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Clinical Significance of a Single *Staphylococcus lugdunensis*-Positive Blood Culture[▽]

Coagulase-negative staphylococci (CoNS) cause human infections that characteristically involve indwelling medical devices with an infection course that is usually indolent. In contrast, *Staphylococcus lugdunensis* is a species of CoNS that can cause infection of either a device or native tissue with an aggressive clinical course more reflective of infection due to *Staphylococcus aureus* (4, 5). The majority of infections caused by *S. lugdunensis* involve skin and soft tissue (8, 9). A panoply of other syndromes are caused by this organism and include endocarditis, septic shock, peritonitis, osteomyelitis, spondylodiscitis, septic arthritis, epidural abscess, brain abscess, and an array of prosthetic device (artificial joint, heart valve, ventriculoperitoneal shunt, and vascular device) infections (6, 7, 10, 11).

The clinical significance of *S. lugdunensis* when only one of multiple blood culture sets is positive is largely undefined; this organism is a skin commensal that can cause, similarly to many other species of CoNS, contamination of blood cultures. To date, three published studies (1, 2, 13) have examined the clinical significance of *S. lugdunensis* in blood cultures. Ebright et al. performed a retrospective cohort study of consecutive patients with two or more blood cultures positive for *S. lugdunensis* at one of five Detroit Medical Center hospitals between January 1990 and May 2002 (2). A total of 21 patients were identified, and only 6 had clinically significant bacteremia. They did not evaluate, however, patients with only one set of blood cultures that grew *S. lugdunensis*.

A retrospective analysis of patients with *S. lugdunensis* bacteremia at three tertiary care centers in Switzerland has also been reported (13). A total of 28 patients with *S. lugdunensis* bacteremia were identified, all of whom had at least two positive blood cultures and 13 of whom had endocarditis; 15 patients with one to five positive blood cultures did not have endocarditis. The clinical features of patients with only one positive blood culture were not described.

In a recently published study in this journal, Choi et al. found that 63 of 1,117,598 patient admissions to seven medical centers had *S. lugdunensis* bacteremia, with an incidence of 5.6 patients per 100,000 admissions. Only 15 patients had clinically significant bacteremia (14 patients with ≥2 separate blood cultures and 1 patient with one positive blood culture and another positive culture from a "sterile" site). The clinical and laboratory characteristics and outcomes of the remaining 48 patients, however, were not described (1).

None of the three studies (1, 2, 13) focused on patients with a single positive blood culture which is usually considered due to skin flora contamination, particularly in patients with no indwelling cardiovascular medical device. Does this assumption change if a CoNS isolate in one positive blood culture is identified as *S. lugdunensis*? In addition to its relevance to direct patient care, this issue is of interest to clinical microbiology laboratories that report blood culture contamination rates. We therefore examined outcomes of patients with a single *S. lugdunensis*-positive blood culture. Among 5,784 cases with a single positive CoNS blood culture at Mayo Clinic Rochester between 1 January 2001 and 24 January 2008, 29 had *S. lugdunensis* isolated. *S. lugdunensis* was detected by testing all CoNS isolates from blood cultures with ornithine decarboxylase and pyrrolidonyl arylamidase.

The median patient age was 63 years (range, 22 to 91 years). Sixteen (55%) episodes occurred in males. In the initial review of medical records, positive blood culture results were not acknowledged by clinicians in 14 (48%) cases, were considered representative of contamination in 6 (21%) cases, and were considered clinically significant bacteremia in only 9 (31%) cases.

The definition of clinically significant bacteremia, especially in the setting of bacteremia caused by CoNS, remains controversial and difficult to standardize. We used the criteria of Souvenir et al. (12) to retrospectively reclassify our cases. Patients were considered to have clinically significant bacteremia if they had one or more of the following: prolonged fever (temperature ≥38°C), hypotension (systolic blood pressure <90 mm Hg), leukocytosis or neutropenia with a left shifted differential, or disseminated intravascular coagulopathy. In addition, a major risk factor for potential infection caused by skin flora was required, including either long-term intravascular catheterization, peritoneal dialysis or hemodialysis, or extensive postsurgical infections with CoNS. Patients were considered to have indeterminate bacteremia if they had a major risk factor with minimal or transitory clinical symptoms. Blood cultures were considered contaminated if patients had an insignificant febrile episode with no significant risk factors; had significant risk factors but were shown by prior, concurrent, or subsequent blood cultures to have a septic episode with an unequivocal pathogen; or had infectious or noninfectious shock-like complications associated with an inconsistent CoNS etiology (e.g., aspiration pneumonia or acute respiratory distress syndrome, respectively).

We reclassified 16 (55%) bacteremias as being caused by a possible contaminant or indeterminate bacteremia (Table 1). Bacteremia was considered clinically significant in 13 (45%) cases (Table 2), with 77% of cases associated with fever, 31% with neutropenia, and 31% with leukocytosis; these proportions were 25%, 0%, and 62%, respectively, in the contaminant or indeterminate bacteremia group. A possible source was identified in 77% of patients with clinically significant bacteremia (central venous catheter [38%], lower extremity cellulitis/ulcer [23%], abdominal surgery [8%], and infected right femoral graft [8%]). Malignancy was identified in 54% of patients with clinically significant bacteremia and in 24% of the other group.

Twenty-seven (93%) patients received antibiotics for a median duration of 14 days (range, 3 to 56 days) with a β-lactam and/or vancomycin in 9 (33%) and a fluoroquinolone in 18 (67%) cases. Details regarding antibiotic administration are shown in Tables 1 and 2. Patients considered to have clinically significant bacteremia received a longer duration of treatment, with antibiotics administered for a minimum of 7, a mean of 33, a median of 15, and a range of 7 to 50 days compared to a mean of 10, a median of 10, and a range of 0 to 28 days in the contaminant or indeterminate group. In the latter group, 7 (44%) of 16 patients received five or fewer days of treatment and 2 were not treated. Echocardiography was performed in four patients (three in the clinically significant bacteremia group and one in the contami-

TABLE 1. Characteristics of patients with a single positive blood culture for *S. lugdunensis* considered a contaminant or indeterminate bacteremia[a]

Case no.	Age (yr), gender	Comorbidities	Fever	Leukocytosis/ leukopenia	Acknowledgment in the medical records/retrospective assessment by reviewers	Alternative diagnosis	CVC	Antibiotic(s) (duration in days)
1	64, F	Metastatic lung cancer	No	Yes/no	Contaminant/contaminant	Pneumonia	No	Gatifloxacin (28)
2	55, M	Morbid obesity, HTN	Yes	No/no	Contaminant/contaminant	UTI	No	Levofloxacin (10)
3	81, M	Prostate cancer, HTN, bronchiectasis	No	Yes/no	Contaminant/contaminant	URI	No	Levofloxacin (10)
4	91, F	DM, stroke, seizures	No	Yes/no	Contaminant/contaminant	Seizure (noninfectious)	No	Ceftriaxone (2), vancomycin (4)
5	59, F	Non-Hodgkin's lymphoma, chemotherapy	Yes	No/no	Contaminant/indeterminate	BC during apheresis for BMT	Yes	None
6	85, F	HTN, stroke	No	Yes/no	NA/contaminant	Aspiration pneumonia	No	Levofloxacin (14)
7	78, F	Cryptogenic cirrhosis, esophageal varices with bleeding, HTN, CKD, DM	No	Yes/no	NA/contaminant	Aspiration pneumonia	No	Levofloxacin (14)
8	86, M	Seizure, HTN, hyperlipemia	No	Yes/no	NA/contaminant	Thalamic infarct	No	Ampicillin/sulbactam (3)
9	34, F	Neurogenic bladder, nephrolithiasis, chronic UTI	Yes	Yes/no	NA/contaminant	*Proteus mirabilis* UTI	Yes	Vancomycin (7), gentamicin (11), cephalexin (15)
10	22, F	Preeclampsia, artificial rupture of membranes	No	Yes/no	NA/contaminant	*Streptococcus viridans* bacteremia	No	Vancomycin (4), gentamicin (4), cephalexin (7)
11	68, M	Laparoscopic adrenalectomy, AFib, HTN	No	Yes/no	NA/contaminant	Pneumonia	No	Piperacillin-tazobactam (7), amoxicillin-clavulanate (7)
12	75, M	Squamous cell lung cancer, hematuria	No	No/no	NA/contaminant	Dizziness, fatigue due to lung cancer	Yes	None
13	49, F	Hodgkin's lymphoma	No	Yes/no	NA/contaminant	*Escherichia coli* UTI	No	Levofloxacin (4)
14	60, F	CKD, hemodialysis, light chain disease, on immunosuppressants	No	No/no	NA/contaminant	BC during stem cell mobilization	Yes	Cefazolin (3)
15	38, F	RA on prednisone, alcoholism, fulminant hepatic failure	Yes	No/no	NA/indeterminate	Hepatitis, *Moraxella nonliquefaciens* bacteremia	Yes	Meropenem (15), vancomycin (15)
16	58, F	Morbid obesity, NASH, Parkinson's disease	No	No/no	NA/contaminant	*Enterococcus* UTI	No	Ampicillin (5)

[a] Abbreviations: F, female; M, male; CVC, central venous catheter; HTN, hypertension; UTI, urinary tract infection; URI, upper respiratory infection; DM, diabetes mellitus; BC, blood cultures; BMT, bone marrow transplant; NA, not acknowledged; CKD, chronic kidney disease; AFib, atrial fibrillation; RA, rheumatoid arthritis; NASH, nonalcoholic steatohepatitis.

TABLE 2. Characteristics of patients with a single positive blood culture for *S. lugdunensis* considered a clinically significant bacteremia[a]

Case no.	Age (yr), gender	Comorbidities	Fever	Leucocytosis/ leucopenia	Acknowledgment in the medical records/ retrospective assessment by reviewers	Possible source	CVC	Antibiotic(s) (duration in days)
1	57, M	Multiple myeloma, CKD, HTN	Yes	No/yes	Bacteremia/bacteremia	None identified	No	Vancomycin (4), clindamycin (7)
2	66, M	PVD, testicular cancer (chemotherapy, radiation)	Yes	No/no	Bacteremia/bacteremia	Infected right femoro-femoral bypass	No	Cefazolin (50)
3	72, M	Recurrent cellulitis, PVD, lymphedema	Yes	No/no	Bacteremia/bacteremia	Lower-extremity cellulitis	No	Cefazolin (7), ceftriaxone (12)
4	65, F	HTN, DM	No	No/no	Bacteremia/bacteremia	None identified	No	Vancomycin (5), ceftriaxone (42)
5	30, M	Lymphedema, lower-extremity infected ulcer	No	Yes/yes	NA/bacteremia	Lower-extremity infected ulcer	No	Ciprofloxacin (13), piperacillin-tazobactam (12)
6	63, M	Cirrhosis from alcohol, DM	Yes	No/no	Bacteremia/bacteremia	Line-related bacteremia	Yes	Vancomycin (7)
7	64, F	Recurrent rectal cancer	Yes	Yes/no	NA/bacteremia	Abdominoperineal resection of rectal cancer	No	Piperacillin-tazobactam (14)
8	89, M	HTN, resuscitated cardiac arrest	Yes	Yes/no	Bacteremia/bacteremia	Line-related bacteremia	Yes	Levofloxacin (14)
9	64, M	Acute myeloid leukemia	Yes	No/yes	Bacteremia/bacteremia	Line-related bacteremia	Yes	Cefepime (17)
10	60, M	Diabetic foot osteomyelitis	No	Yes/no	NA/bacteremia	Diabetic foot osteomyelitis requiring transmetatarsal amputation	No	Levofloxacin (20), metronidazole (20)
11	30, M	Cutaneous anaplastic large T-cell lymphoma	No	Yes/no	Bacteremia/bacteremia	Line-related bacteremia	Yes	Vancomycin (14)
12	53, F	Metastatic leiomyosarcoma	Yes	No/yes	Bacteremia/bacteremia	None identified	No	Cefepime (6)
13	54, M	Relapsed extramedullary myeloid sarcoma, BMT on immunosuppression	Yes	No/yes	Contaminant/bacteremia	Line-related bacteremia	Yes	Vancomycin (4), levofloxacin (52 while neutropenic)

[a] PVD, peripheral vascular disease; other abbreviations are defined in Table 1, footnote *a*.

nate group), and no evidence of endocarditis was seen in any of them. Twenty-one (72%) patients had follow-up blood cultures, and all were negative. No patient suffered a complication or relapse of *S. lugdunensis* bacteremia with >3 months of follow-up.

Favre et al. examined the clinical significance of single blood cultures positive for CoNS at their institution (3). Over a period of 3 years, 411 positive cultures for CoNS were identified, of which 163 (40%) were single positive blood cultures. While the treating physicians considered 69% of single positive blood culture for CoNS to be contaminated, no analysis of the data according to the criteria of Souvenir et al. (12) was performed, so it is not possible to directly compare our findings with theirs.

To our knowledge, this is the first study to evaluate the clinical significance of a single positive blood culture due to *S. lugdunensis*. This presentation was uncommon in our clinical practice and not even acknowledged by clinicians in the medical records in almost 50% of cases. Although *S. lugdunensis* can cause severe infections with bacteremia akin to those caused by *S. aureus*, it can also cause blood culture contamination like other CoNS and clinical correlation is key in making management decisions. The observation that clinically significant bacteremia caused by *S. lugdunensis* occurred in 45% of cases with single positive blood cultures suggests that clinical laboratories should screen all blood culture isolates of CoNS for *S. lugdunensis* and that isolation of this organism in a single set of blood cultures should not necessarily result in its classification as a contaminating organism.

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